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KIM

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/464,158	12/16/99	SUNDREHAGEN E	697.011US1

021186 HM22/0323
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EXAMINER	
HINES, J	
ART UNIT	**PAPER NUMBER**
1645	6

DATE MAILED: 03/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/464,158	Sundrehagen
Examiner	**Group Art Unit**
Ja-Na Hines	1645

☒ Responsive to communication(s) filed on *Dec 16, 1999*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-12* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-12* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☒ The proposed drawing correction, filed on *Dec 16, 1999* is ☒ approved ☐ disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *6*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Specification

1. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

2. The use of the trademark WHARTMAN QASL ™ and other diagnostics and reagents have been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

3. Claims 3-12 are objected to under 37 CFR 1.75© as being in improper form because the dependant claims are dependant upon other multiple dependent claims. See MEP. § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is unclear in the recitation of "the assessment of alcohol consumption". It is unclear whether the assessment will assess how much alcohol a person has had or assess whether the carbohydrate-free transferrin is present only in alcoholics consumption, or assess when only high levels of alcohol are consumed.

5. Claim 1 is vague and indefinite in the recitation of "carbohydrate-free transferrin". It is unclear how to define such as term. Neither the specification nor the claims recite a specific protein. The carbohydrate-free transferrin is not defined by a specific structure, isoelectric point, or molecular weight. The examples in the specification does not teach which known transferrin proteins meet or do not meet the qualification of being deemed carbohydrate-free transferrin. The claims do not recite how to determine whether a transferrin protein is carbohydrate free. Therefore the term carbohydrate-free transferrin, without a defining characteristics in unclear.

6. Claim 2 is vague, the term "derived" which relates to a blood-derived sample being used is indefinite. It is unclear what characteristics will be retained by the derivation of a blood-derived sample. The specification does not provide any guidance for the derivation of a blood-derived sample. The specification does not teach how the derivation of a blood-derived sample will occur and how much of the original blood must be retained by the derivation procedures. Therefore, the use of "derived" sample is unclear.

7. Claims 3 and 5 are vague and indefinite. The claim recites "fragments thereof" and "mixtures thereof". It is unclear how to define the metes and bounds of these terms. It is unclear whether fragments thereof includes any type of antibody fragments or some other types of fragments. Further, it is unclear how to define "mixtures thereof". There is no definition which states what mixtures are capable of being used as binding ligands. Also, it is unclear how to make mixtures thereof without any defined parameters, therefore the claim is unclear.

8. Claim 4 is vague in the recitation of "different lectins". The metes and bounds of different lectins is quite broad, therefore it is unclear which different lectins can be used in the method. Therefore the claim is unclear.

9. Claim 5 recites alternative limitations which are improperly expressed. "Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. One acceptable form of alternative expression, which is commonly referred to as a Markush group recites members as being 'selected from the group consisting of A, B and C'." Another acceptable form recites "selected from 1, 2, 3, or 4." Applicant may correct this by amending the claim to recite the appropriate language.

10. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MEP.

§ 2172.01. The omitted steps in claim 1 are there is no contact step which contacting the remaining carbohydrate free transferrin for detection, there is no detection step which states how the transferrin is detected, and there is is no correlation step which states the once the content of transferrin is determined, how to assess for alcohol consumption.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-3, 6-8 and 10-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Sundrehagen (WO 91/19983). Sundrehagen teaches assessing the concentration of a subset of analyte variants within a group of different analyte variants and test kits and reagents composition for use in such method (page 1 lines 5-9). The assessment of the level of different variants of the protein transferrin in serum is of particular importance (page 2 lines 13-15). Transferrin generally occurs in sialylated forms, however in chronic alcohol abusers, desialylated transferrin, such as transferrin carrying two or less sialyl residues, is relatively increased in content when compared to non-alcoholics (page 2 lines 15-23). Desialylated transferrin is often called Carbohydrate Deficient Transferrin (CDT) and is considered a clinically reliable marker for chronic alcoholism

(page 2 lines 23-25). The present invention is based on the concept that proteinaceous analyte variants can be labeled prior to separation using labeled binding partners so that after separation assessment of the label in the separated fractions provides a quantitative indication of the relative abundance of the variants (page 4 lines 25-30). This procedure is substantially simpler in operation than prior systems using separation followed by conventional immunoassays (page 4-5 lines 37-3). The method if assessment of the concentration of a subset of variants in a population of proteinaceous analyte variants capable of separation by fractionation system (page 5 lines 5-17). Also taught as analytical test kit comprising compositions with reagents and/or materials required to perform the fractionation (page 6 lines 4-8). The analyte variants differ according to their charge in a given buffer system and they can be easily separated by a charge-based system such as ion exchange chromatography or electrophoresis (page 6 lines 8-10). The use immunoreactive antibody fragments such as Fab, or F(v) fragments can be used in the method (page 8 lines 6-24). Anti-transferrin antibodies are especially useful in transferrin variant analysis (page 9 lines 24-26). This method is particularly suited for analysis levels of different transferrin (page 8 lines 35-37). The method of assessment of variants of transferrin can be found in blood plasma, serum, whole blood or hemolysate (page 9 lines 1-3). The advantage of the combination of immunological quantitation and fractionation in one operation obtained by separating the complexes is that it is possible to measure transferrin and other variants far more easily , in particular transferrin with low sialic acid content in the blood pf a person undergoing investigations related to alcohol consumption (page 14 lines 15-20). Fraction can occurs using

methods such as chromatography, electrophoresis, and filtration (page 6-7 lines 7-3). T test kit for use in transferrin analysis can comprise labeled anti-transferrin antibodies, other labeled antibodies or other proteinaceous binding partners (page 10 lines 28-35). Example 2 discloses analysis of samples of sera from alcohol abusers and non-drinkers. Examples 7-8 teach assessment of desialylated transferrins in sera from patients. Examples 9-10 discloses a test for desialylated transferrin (CDT) in serum.

Therefore, Sundrehagen teaches the invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 4-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sundrehagen (WO 91/19983) in view of Pekelharing et al., (Analytical Biochem). Sundrehagen (WO 91/19983) has been discussed above, however, Sundrehagen does not teach the use of lectins as carbohydrate binding ligands. Pekelharing et al., teaches lectin-enzyme immunoassay of transferrin sialovariants using immobilized antitransferrin and enzyme labeled galactose binding lectin from *Ricinus communis*. The ELISA assay was modified by replacing the immobilized antibody or enzyme linked antibody with a lectin or other carbohydrate binding protein; thus is was possible to

create a heterologous lectin-enzyme immunoassay system (LEIA) (page 320). The sandwich assay can consists of a lectin and an antibody where the lectin can replace either the immobilized or the enzyme-linked antibody used in the ELISA (page 321). The lectin chosen was from *Ricinus communis* because it is one of the galactose-binding lectins precipitating asialo-transferrin (page 321). However another lectin considered was the isolated lectin from *Crotalaria juncea* seeds (page 325). Increased desialotransferrin concentrations were found in the serum from alcoholics (page 325). Materials and Methods section teaches affinity purification of rabbit antitransferrin IgG on immobilized transferrin, and the lectin enzyme immunoassay protocol (page 322). The LEIA has increased sensitivity when subfractions are to quantitated, it increases the captured proteins, and increases binding affinity (page 324). Further advantages include speed, specificity and simplicity when microtiter plates are used (page 324).

Therefore it would have been obvious at the time of applicants invention to use a modified ELISA by replacing the immobilized antibody or enzyme linked antibody with a lectin or other carbohydrate binding protein of Pekelharing et al., (Analytical Biochem) in the method of assessment of alcohol consumption as taught by Sundrehagen, because Pekelharing et al., teaches that the use of lectins increases the speed, specificity, sensitivity and simplicity of an immunoassay.

13. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sundrehagen (WO 91/19983) in view of Dreher et al., Canadian Patent 2,074,345. Sundrehagen (WO 91/19983) has

been discussed above, however, Sundrehagen does not teach the use of the determination of transferrin by turbidometric or nephelometric means. Dreher et al., teaches methods and agents for the turbidimetric or nephelometric determination of analytes in liquids with the aid of an antibody binding reaction (page 1 lines 2-4). The immunoturbidimetry and immunonephelometry are based on the interaction between antibodies and the detected antigen. The interaction results in the formation of high molecular weight aggregates which act as centers for scattering incident light; the light is recorded as an increase in extinction in immunoturbidimetry and as an increase in the intensity of scattered light relative to the incident light in immunonephelometry (page 1 lines 10-18). This method can be used to determine antigens and proteins including transferrin (page lines 29-34). Example 2 teaches turbidimetric immunoassay with anti-transferrin antibody fragments. The great advantage of the immunoturbidimetry and immunonephelometry is that is can be automated relatively simply (page 1 lines 25-28).

Therefore, is no more then routine skill would have been required to use well known methods for transferrin determination using immunoturbidimetry and immunonephelometry techniques as taught by Dreher et al., in the method of assessment of transferrin as taught by Sunderhagen, because immunoturbidimetry and immunonephelometry means can be easily and simply automated.

Prior Art

14. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US Patent 4,626,355 teaches methods of determining alcohol consumption separating

isotransferrin variants. US Patent 5,702,904 teaches immunoassays for identifying alcoholics and monitoring alcohol consumption. Dumon et al., teaches chronic alcohol abuse increases serum concentrations of sialic acid deficient isoforms of disialo, monosialo and asialo transferrin. Pekelharing et al., (A2 Iron Binding Proteins) teaches an ELISA technique for measurement of transferrin glyco-variants in body fluids using lectins bound to a solid phase.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is (703) 305-0487. The examiner can normally be reached on Monday through Thursday from 6:30am to 4:00pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Ja-Na Hines

March 21, 2001

JENNIFER E. GRASER
PRIMARY EXAMINER